

Remarks

Claims 1-7, 16, 23, 26 and 31-40 are pending, with claims 1-4 being the independent claims. Claims 3-7, 23, 26, 31, and 33-40 are withdrawn from consideration by the Examiner as being drawn to non-elected inventions, but remain pending. Claims 16 and 32-34 have been amended. Support for the amendments may be found throughout the specification and in the claims as originally filed. The specification has been amended to reflect sequence identifiers for the sequences described throughout the specification, to remove an embedded hyperlink, and to incorporate by reference the submission of the substitute sequence listing filed herewith. These changes are believed to introduce no new matter, and their entry is respectfully requested.

In compliance with the Notice to Comply mailed September 17, 2009 ("Notice"), Applicants submit herewith a computer readable copy of the substitute sequence listing on compact disc. The computer readable copy of the substitute sequence listing is labeled "Computer Readable Format," and replaces the original computer readable copy of the sequence listing filed on September 28, 2005. In accordance with 37 C.F.R. §§ 1.52(e)(4) and 1.821(g), Applicants' attorney hereby states that the substitute sequence listing does not include new matter.

Applicants also submit herewith duplicate copies of the substitute sequence listing on compact discs labeled "Copy 1" and "Copy 2." Each compact disc containing the substitute sequence listing is formatted for IBM-PC, MS-Windows, and ASCII DOS text. Each disc contains one file: "Final Sequence Listing.txt," 6,125,826 bytes, created on January 19, 2010.

In compliance with 37 C.F.R. § 1.52(e)(4), Applicants' attorney hereby states that the computer readable copy of the substitute sequence listing and the duplicate copies of the substitute sequence listing are identical.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 16 and 32 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, is respectfully traversed. The Examiner states that "[c]laims 16 and 32 are indefinite in the recitation of 'spp.' [b]ecause it is not clear what is meant. (In addition, note that 'spp' after 'Histoplasma' does not have a period)." Office Action, page 3. Applicants respectfully disagree.

As shown above, claims 16 and 32 have been amended to include a period in the term 'spp' after '*Histoplasma*.' However, Applicants respectfully submit that "spp." is a well known abbreviation for the term "species." "Cell Structure and Taxonomy," in *Burton's Microbiology for the Health Sciences*, Engelkirk, P.G. and Burton, G.R.W., eds. Lippincott Williams & Wilkins, Baltimore, MD, p. 40 (2006). A person of ordinary skill in the art would have understood that "*Coccidoides spp.*," "*Histoplasma spp.*," "*Plasmodium spp.*," "*Trypanosoma spp.*," "*Schistosoma spp.*," and "*Leishmania spp.*" as recited in claims 16 and 32 represent all members of the *Coccidoides* species, the *Histoplasma* species, the *Plasmodium* species, the *Trypanosoma* species, the *Schistosoma* species, and the *Leishmania* species, respectively. However, not in
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acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended the claims to recite "species" rather than "spp." Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 102(a)

The rejection of claims 1, 2, 16, and 32 under 35 U.S.C. § 102(a) as allegedly being anticipated by De Groot *et al.*, *Immun. Cell Biol.* 80:255-269 (2002) ("De Groot") is respectfully traversed. A claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), cert denied, 465 U.S. 1026 (1984). Applicants respectfully assert that De Groot does not teach every limitation of claims 1, 2, 16, and 32, and therefore does not anticipate these claims.

Claims 1, 2, 16, and 32 are directed to a method of identifying candidate epitopes that induce a HLA class I CTL response against variants of said peptide epitope. The method of each of claims 1, 2, 16, and 32 comprises identifying, *from a particular antigen* of an infectious agent, variants of a peptide epitope 8-11 amino acids in length. In contrast, De Groot allegedly teaches "comparing the sequence of 8-11-mer peptides across strains of infectious agents such as HIV-1 to identify broadly conserved (cross-clade) epitopes. . . ." Office Action, page 3. De Groot does not disclose using a single epitope as a starting point and identifying variants of the single epitope, as required by the present invention. Thus, Applicants respectfully assert that De Groot does not teach each and every element of claims 1, 2, 16, and 32. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 103(a)

The rejection of claims 1, 2, 16, and 32 under 35 U.S.C. § 103(a) as allegedly being obvious over De Groot is respectfully traversed.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 745 F.2d 1468, 1471-73 (Fed. Cir. 1984). As set forth in *Graham v. John Deere Co. of Kansas City*, "[u]nder § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined." 383 U.S. 1, 17 (1966). This has been the standard for over 40 years, and remains the law today. *See KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1734 (2007). If, after these criteria are considered, the evidence indicates that the claimed invention is obvious over the prior art, it may be said that a *prima facie* case of obviousness have been established.

Applicants respectfully assert that the Examiner has not met the burden of establishing a *prima facie* case of obviousness because a person of ordinary skill in the art would not have arrived at the claimed invention based on the teachings of De Groot. As discussed above, De Groot does not disclose a method for identifying variants of a single peptide epitope, as required by the present invention. In addition, the methodology of De Groot and the present invention yield identifiably distinct results. The claimed methodology may be used to identify specific CTL epitopes that are likely

to induce broad immune responses. Starting with a single peptide epitope, variants of the peptide epitope are identified, wherein the variant comprises primary anchor residues of the same HLA class I binding motif. The present invention then identifies a variant(s) that comprises only conserved non-anchor residues in comparison to at least one remaining variant. The resulting variant is a candidate peptide for use in vaccine development. A product of the multiple levels of screening required by claims 1, 2, 16, and 32, the resulting variant may induce a CTL response against other variants of the peptide epitope. In contrast, De Groot sought to identify any putative CTL epitope within the HIV genome. At best, De Groot discloses identifying conserved regions within a studied HIV population, wherein the conserved regions are putative CTL epitopes. The methodology disclosed in De Groot does not necessarily identify a candidate peptide epitope(s) that is able to induce a CTL response against variants of the peptide epitope.

Finally, the Examiner has not provided a rationale for modifying the methodology of De Groot to arrive at the present invention. Without an express teaching of the invention and without motivation to modify the methodology of De Groot, a person of ordinary skill in the art would need to possess some level of prescience to arrive at the present invention. Although a person of ordinary skill in the art possesses "ordinary creativity" (KSR, 127 S.Ct. at 1742), the standard of obviousness under *KSR* does not require a person of ordinary skill in the art to possess any level of prescience.

Applicants respectfully assert that the Examiner has not provided sufficient factual basis for concluding that the present invention would have been obvious to a person of ordinary skill in the art. Therefore, for at least the above reasons, the Examiner

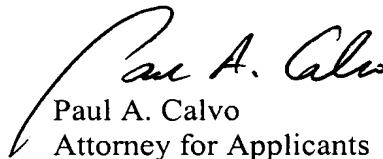
has not established a *prima facie* case of obviousness. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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